

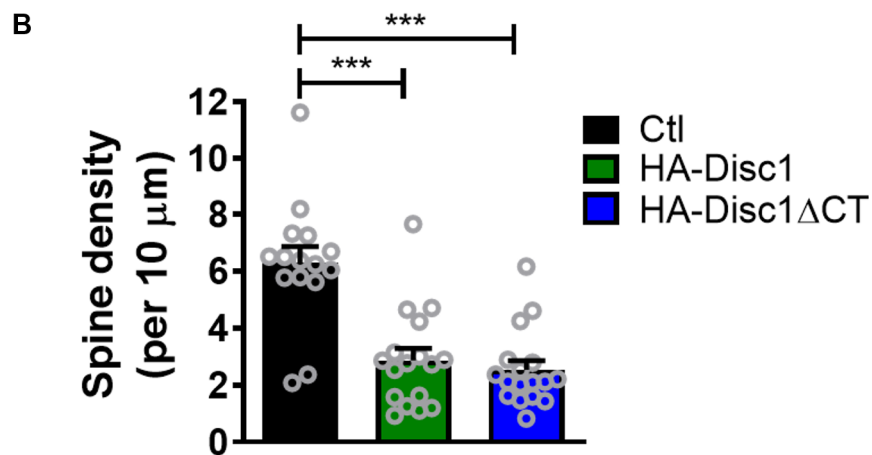
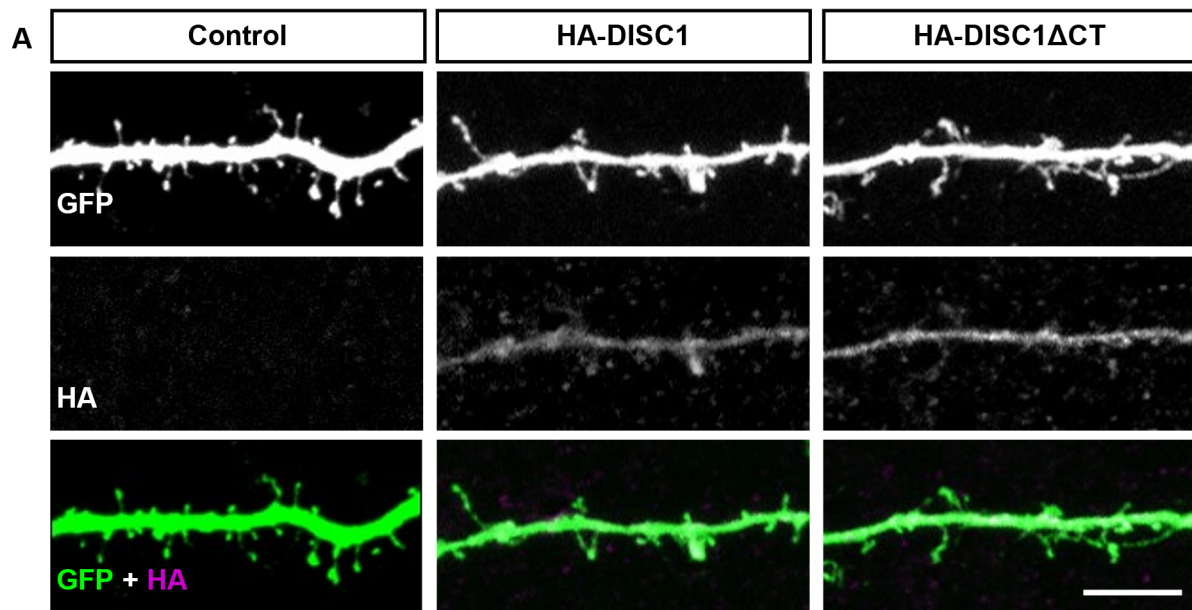
# **Estradiol reverses excitatory synapse loss in a cellular model of neuropsychiatric disorders**

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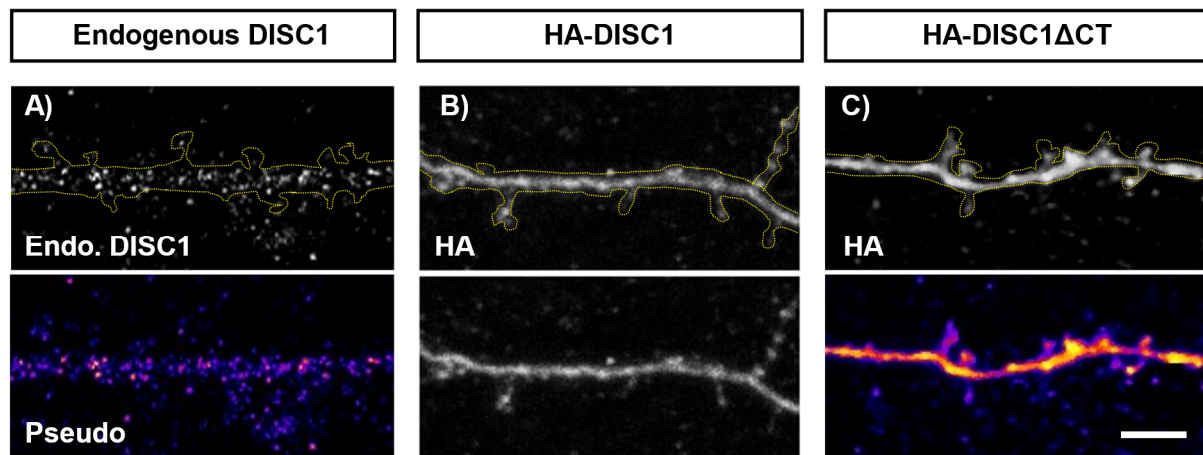
**Supplemental Material:**

**Supplemental Figures**



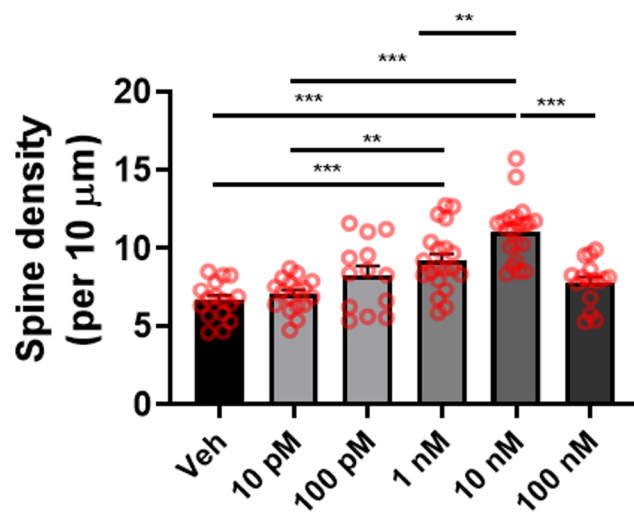
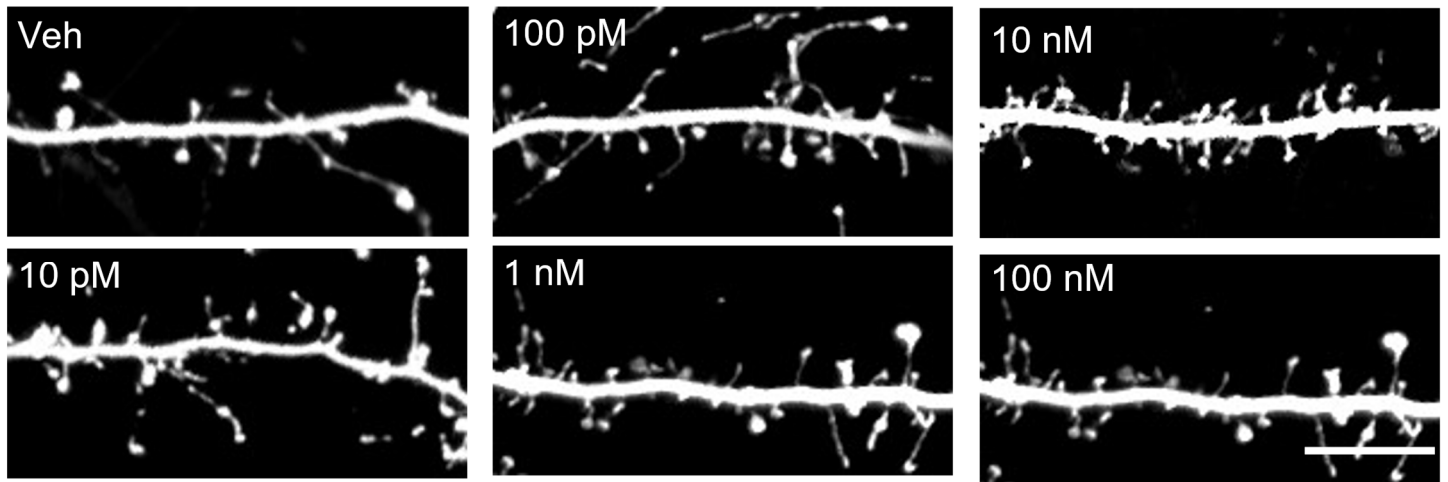
**Supplemental Figure 1. Full length and C-terminal truncated DISC1 induces spine loss in primary cortical neurons.**

**(A)** Representative images of cortical neurons (DIV 26) transfected with GFP alone, GFP + HA-DISC1 or GFP + HA-DISC1 $\Delta$ CT. **(B)** Quantification of spine linear density. Overexpression of HA-DISC1 causes a reduction of spine density as previously reported; exogenous expression of DISC1 $\Delta$ CT also causes a reduction in spine linear density (dendritic spine linear density/10  $\mu$ m): control, 6.3 $\pm$ 0.6; HA-DISC1, 2.87 $\pm$ 0.42; HA-DISC1 $\Delta$ CT, 2.54 $\pm$ 0.34). Scale bar = 5  $\mu$ m.

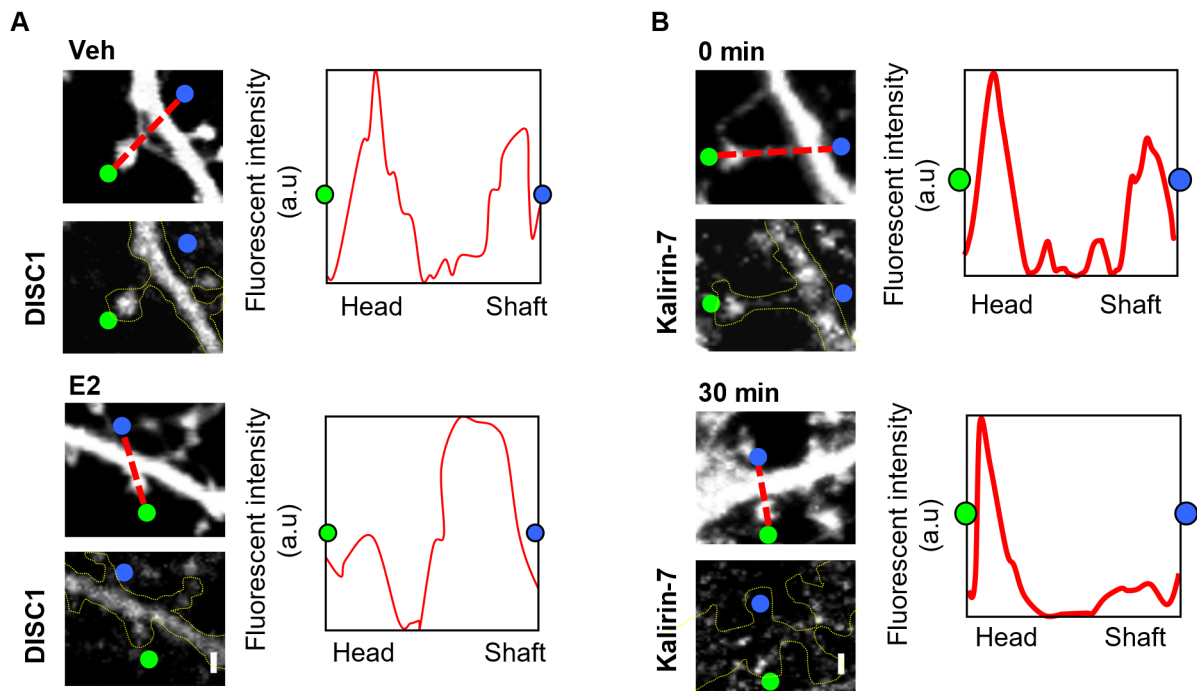


**Supplemental Figure 2. Full length and C-terminal truncated DISC1 aggregates within dendrites of cortical neurons.**

Representative images of cortical neurons (DIV 26) transfected with GFP alone, GFP + HA-DISC1 or GFP + HA-DISC1 $\Delta$ CT. **(A)** Endogenous DISC1 could be observed in discrete punctate structures within dendrites and juxtaposed to dendrites. In comparison, both wildtype and  $\Delta$ CT forms of DISC1 were found to aggregate within dendrites. Scale bar = 5  $\mu$ m.



**Supplemental Figure 3. 17 $\beta$ -estradiol increases dendritic spine density in a dose-response manner.** Primary cortical neuron expressing GFP were treated with 17 $\beta$ -estradiol at range of concentrations for 30 minutes. Following fixation and immunocytochemistry, dendritic spine linear density was assessed. Treatment with 1 or 10 nM 17 $\beta$ -estradiol increased spine linear density significantly; 10 or 100 pM as well as 100 nM 17 $\beta$ -estradiol did not alter spine density significantly compared to vehicle treated control neurons. Scale bar = 5  $\mu\text{m}$ .



**Supplemental Figure 4. Estradiol induced trafficking of DISC1 and kalirin-7. (A)**

High magnification of areas highlighted by yellow dashed boxes in **Figure 3C**; line scan of DISC1 staining within spine heads further demonstrates a redistribution of DISC1 from spines to dendritic shaft after E2 treatment. **(B)** High magnification of areas highlighted by yellow dashed boxes in **Figure 3E**; line scan of kalirin-7 distribution within spine heads reveals an enrichment of kalirin-7 within spine heads after E2 treatment. Scale bar = 1  $\mu\text{m}$ .